Hard tissue changes after guided bone regeneration of peri-implant defects comparing block versus particulate bone substitutes: 6-month results of a randomized controlled clinical trial

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Abstract: OBJECTIVES To test whether block bone substitute used for guided bone regeneration (GBR) of peri-implant defects leads to different thickness of the augmented hard tissue than particulate bone substitute. MATERIAL AND METHODS In 24 patients, 24 two-piece dental implants were placed >4 months after tooth extraction. Following random allocation, 12 peri-implant bone dehiscences were grafted with an individually shaped block of deproteinized bovine-derived bone mineral (DBBM) and 12 bone dehiscences with particulate DBBM. All the sites were covered with a collagen membrane stabilized with resorbable pins. Immediately after wound closure and after 6 months, the horizontal thickness (HT) of the augmented hard tissue was measured at the level of implant shoulder using cone beam-computed tomography. RESULTS After wound closure, the median HT measured 3.35 mm (mean: 3.38) in the block group and 2.85 mm (mean: 2.73) in the particulate group. At 6 months, the median HT decreased to 2.90 mm (mean: 2.71) in the block group and to 0.2 mm (mean: 0.52) in the particulate group. This difference was statistically significant ($p < .001$). CONCLUSIONS Block bone substitute used for GBR of peri-implant defects was superior to particulate bone substitute regarding the dimension of the augmented hard tissue after 6 months of healing.

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Hard tissue changes after guided bone regeneration of peri-implant defects comparing block versus particulate bone substitutes: 6 month-results of a randomized controlled clinical trial

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Abstract

Objectives: To test whether block bone substitute used for guided bone regeneration (GBR) of peri-implant defects leads to different thickness of the augmented hard tissue than particulate bone substitute.

Material & Methods: In 24 patients, 24 two-piece dental implants were placed >4 months after tooth extraction. Following random allocation, 12 peri-implant bone dehiscences were grafted with an individually shaped block of deproteinized bovine-derived bone mineral (DBBM) and 12 bone dehiscences with particulate DBBM. All the sites were covered with a collagen membrane stabilized with resorbable pins. Immediately after wound closure and after 6 months, the horizontal thickness (HT) of the augmented hard tissue was measured at the level of implant shoulder using cone beam computed tomography.

Results: After wound closure, the median HT measured 3.35 mm (mean: 3.38) in the block group and 2.85 mm (mean: 2.73) in the particulate group. At 6 months, the median HT decreased to 2.90 mm (mean: 2.71) in the block group and to 0.2 mm (mean: 0.52) in the particulate group. This difference was statistically significant ($p<0.001$).

Conclusions: Block bone substitute used for GBR of peri-implant defects was superior to particulate bone substitute regarding the dimension of the augmented hard tissue after 6 months of healing.

Introduction

Guided bone regeneration (GBR) with particulate bone substitutes in combination with collagen membranes (CM) is currently the most widely used and best documented method for bone augmentation of peri-implant defects. Numerous short-term (Benic, Jung, Siegenthaler, Hammerle, 2009; Mayfield, Skoglund, Nobreus, Attstrom, 1998; Zitzmann, Scharer, Marinello, 2001; Zumstein, Billstrom, Sennerby, 2012) and two recent long-term controlled clinical trials (Benic, Bernasconi, Jung, Hammerle, 2017a; Jung, Fenner, Hammerle, Zitzmann, 2013) document that implants placed simultaneously with GBR perform similarly to implants completely placed into pristine bone with respect to implant survival and interproximal bone levels. Previous cone beam computed tomographic (CBCT) investigations of peri-implant defects treated with particulate deproteinized bovine-derived bone mineral (DBBM) with CM found well-maintained levels of the augmented buccal bone after 5-9 years (Buser, et al., 2013; Jung, Benic, Scherrer, Hammerle, 2015). Moreover, a recent 15-year follow-up clinical investigation with intra-subject control found no differences in the dimension of the buccal bone between implants placed simultaneously with GBR using particulate DBBM and CM compared to implants placed completely into pristine bone (Benic, et al., 2017a).

The main shortcoming of GBR with particulate bone graft in combination with CM is their lack of morphological stability often leading to partial loss of the augmented space. These materials cannot well withstand the soft tissue pressure and compression of the augmented site may result in a displacement of the bone substitute material (Mellonig, Nevins, Sanchez, 1998; Mir-Mari, Benic, Valmaseda-Castellon, Hammerle, Jung, 2017; Mir-Mari, Wui, Jung, Hammerle, Benic, 2016; Schwarz, et al., 2007; Strietzel, Khongkhunthian, Khattiya, Patchanee, Reichart, 2006). Consequently, the use of particulate bone substitute and CM is not optimal for the augmentation of deficient ridge contours (Benic, Hammerle, 2014).

Bone grafts in block form offer improved mechanical support to the covering membrane and the overlying mucosa. Hence, they may lead to better results regarding the augmentation of ridge contours. Previous investigations of bone block substitutes focused on primary ridge augmentations. It was shown that DBBM blocks or equine-derived bone mineral blocks lead to successful horizontal ridge augmentation in both experimental and clinical studies (Araujo, Sonohara, Hayacibara, Cardaropoli, Lindhe, 2002; De Santis, et al., 2012; Hammerle, Jung, Yaman, Lang, 2008; Schwarz, et al., 2010; Schwarz, Mihatovic, Ghanaati, Becker, 2017; Schwarz, et al., 2008).

Recent studies assessed the use of bone substitute blocks for the augmentation of

deficient ridge contours simultaneously with implant placement (Benic, et al., 2017b; Benic, et al., 2016; Mir-Mari, et al., 2016). An in-vitro trial investigated the dimensional stability of the regions augmented with GBR during wound closure (Mir-Mari, et al., 2016). It was found that flap suturing induced a considerable amount of particulate DBBM displacement resulting in a reduction of the horizontal thickness of the augmented site. In contrast, the sites augmented with DBBM blocks exhibited less thickness reduction. On average, the use of block instead of particulate DBBM reduced the amount of thickness reduction at the level of the implant shoulder by more than 50%. A similar beneficial effect was achieved by fixing the membrane with resorbable pins (Mir-Mari, et al., 2016). Based on these in-vitro experiments the in-vivo performance of collagen-containing equine blocks, of DBBM blocks and of particulate DBBM for GBR with simultaneous implant placement was investigated in a recent preclinical study (Benic, et al., 2017b; Benic, et al., 2016). All the grafting materials were applied in combination with CM for the augmentation of box-shaped peri-implant defects. After 4 months of healing, the equine block rendered the most favorable outcomes in hard and soft tissue ridge contours followed by the DBBM block and the particulate DBBM.

The primary aim of the present clinical trial was to test whether DBBM block used for GBR of peri-implant defects leads to different thickness of the augmented hard tissue than particulate DBBM. The results of the histological analysis of the augmented hard tissue will be presented in a subsequent publication.

Materials and methods

This article was prepared according to the CONSORT guidelines for reporting parallel group randomized trials (Moher, et al., 2010).

Study design

This trial was designed as a randomized controlled clinical trial with two parallel study groups and a duration period of five years. The study was performed at the Clinic of Reconstructive Dentistry, Center of Dental Medicine, University of Zurich, Zurich, Switzerland. The trial was approved by the local ethical committee (reference code KEK-ZH 2011-0075; Kantonale Ethik-Kommission, Zurich, Switzerland) and registered in the German Clinical Trials Register (DRKS00005803).

Study population

Twenty-nine subjects were recruited in need of a dental implant in an edentulous jaw region with a buccal deficiency of the alveolar bone. Written informed consent was obtained from all the patients prior to the initiation of treatment.

The subjects had to fulfill the following inclusion criteria:

- At least 18 years of age
- No medical history in which any elective oral surgical intervention would be contraindicated
- No heavy smoking (>20 cigarettes per day), no pipe or cigar smoking
- No active periodontal disease
- Full-mouth plaque score <25%
- Need of a dental implant with a concomitant buccal deficiency of the alveolar ridge
- Implant placement >4 months after tooth extraction
- Presence of a dehiscence-type buccal bone defect after implant placement

Randomization and allocation concealment

The patients were randomly allocated to one of the two treatment modalities according to a computer-generated randomization list. A permuted-block randomization with block sizes of 4 and allocation ratio of 1:1 was applied to generate the allocation sequence. Allocation to the study groups was concealed by means of sealed envelopes until the time of surgical procedure that required GBR of the bone dehiscence.

Treatment procedures and clinical measurements

The investigators participating in the study were experienced in implant placement and bone augmentation procedures. Prior to the study initiation, all investigators attended a training session to standardize the patient selection and the treatment procedures and to calibrate the assessment techniques.

Prior to surgery, the patients received antibiotics (2x750 mg amoxicillin) and non-steroidal analgesics/antiphlogistics. The surgery was performed under local anaesthesia. A crestal and a vertical releasing incision were performed and the mucoperiostal flaps were

elevated. The implant bed was prepared according to the manufacturer's recommendations and a titanium two-piece dental implant (OsseoSpeed EV, DENSTPLY Implants, Mannheim, Germany) was inserted in a prosthetically ideal position. The height of the buccal bone defect was measured with reference to the implant shoulder by using a calibrated periodontal probe. There were 21 one-wall defects and 3 two-wall defects.

The peri-implant bone defects were randomly assigned to receive one of the following GBR treatments:

- *Group particulate bone substitute (particulate):* particulate deproteinized bovine bone mineral (DBBM) (Geistlich Bio-Oss® spongiosa granules, particle size 0.25-1mm, Geistlich Pharma AG, Wolhusen, Switzerland) + native bilayer collagen membrane (NBCM) (Geistlich Bio-Gide®, Geistlich Pharma AG) + resorbable polylactic acid fixation pins (Inion GTR™, Inion Ltd, Tampere, Finland)
- *Group block bone substitute (block):* DBBM block (Geistlich BioOss® block, Geistlich Pharma AG) + NBCM (Geistlich Bio-Gide®, Geistlich Pharma AG) + fixation pins (Inion GTR™, Inion Ltd).

Ten out of 12 (83.3%) particulate sites and 11 out of 12 (91.7%) block sites presented one-wall defects. The remaining sites had two-wall defects.

The peri-implant bone defect was filled and the missing ridge contour was built up with DBBM without autogenous bone. DBBM blocks were shaped with diamond burs and adapted to fit the defect morphology (Fig. 1 and 2). No fixation screws were used. Particulate DBBM was applied to over-augment the buccal and the coronal ridge contours. The horizontal thickness of the grafting material was measured at the level of the implant shoulder by using a periodontal probe. NBCM and DBBM were stabilized by tacking the buccal margin of the membrane onto native bone apically to the defect with 2 or 3 fixation pins. The oral margin of the membrane was inserted under the oral flap. A periosteal-releasing incision was performed in the apical region of the buccal flap to allow tension-free wound closure. Primary wound closure was obtained with non-resorbable monofilament sutures (Gore-Tex®, W.L. Gore & Associates, Flagstaff, AZ, USA).

The patients were instructed to refrain from mechanical plaque removal in the proximity of the surgical site and to rinse the oral cavity twice daily with 0.2% chlorhexidine-digluconate. Antibiotics were prescribed for 5 days (3x750 mg amoxicillin/day) and analgesics (diclofenac 50 mg) according to the individual needs. The sutures were removed

7 days after implant placement. Post-surgical visits included inspection of the site of surgery and supra-gingival cleaning and were performed 1 and 4 weeks after implant placement. At these visits, the soft tissue condition was rated “normal”, “dehisced” or “swollen”.

No soft tissue grafting was performed following implant placement and GBR. At 6 months, re-entry surgery was performed by elevating the buccal mucoperiosteal flap and the augmented hard tissue was assessed (Fig. 1f and 2g). In the presence of bone dehiscence, defect height was measured with reference to the implant shoulder by using a calibrated periodontal probe. Cover screws were replaced by healing abutments and the flaps were sutured.

CBCT scanning and analysis

CBCT scans were taken (1) immediately after implant placement and (2) after 6 months prior to re-entry surgery (Fig. 1-4). CBCT imaging was performed with a 3D Accuitomo 170 scanner (J. MORITA EUROPE GMBH, Dietzenbach, Germany). The scans were made using the following technical parameters: 90 kV, 5 mA, 87.5 mAs, voxel size of 125-250 µm, 360° rotation and scanning time of 17.5 sec.

CBCTs were analyzed by one investigator who was unaware of the specific experimental conditions. A bucco-oral cross-section perpendicular to the implant central axis was used for the CBCT analysis (i-Dixel 2.0 3D Imaging Software, J. MORITA EUROPE GMBH).

The following parameters were assessed on each CBCT scan:

- the horizontal thickness of the augmented hard tissue measured from the implant shoulder in a buccal direction perpendicular to the implant long axis (HT) (Fig. 5)
- the thickness of the augmented hard tissue measured from the implant shoulder in a bucco-coronal direction at 45 degrees to the implant long axis (45°T) (Fig 5).

CBCT analysis was performed twice with a 1 week-period between the measurements. Mean values of the 2 measurements were calculated and used for the statistical analysis.

Statistical analysis

The primary outcome parameter was the horizontal thickness of the augmented hard tissue at 6 months.

The sample size calculation was based on two independent groups, a normal distribution and the two-sample t-test. To detect a difference of 0.5 mm with a standard deviation (SD) of 0.5 mm (power: 80%, significance level: 0.05), 17 patients per group (total of 34 patients) were required. As no clinical data were available for the same combination of materials, the sample size calculation was considered to be of exploratory nature

The data distributions were represented with boxplots and the data were reported with medians, means, standard deviations (SD), interquartile ranges (IQR), and ranges (R software; R Foundation, Vienna, Austria). The non-parametric Wilcoxon Mann–Whitney U-test was applied to detect differences between the groups because of the small size of the included sample. Results of tests with p-values ≤ 0.05 were considered statistically significant. No correction for multiple testing was performed for the analyses of the secondary endpoints.

Results

Patients

Twenty-nine patients were recruited for surgery from August 2014 to July 2017. One block case and two granulate cases were excluded due to the absence of a dehiscence-type bone defect. In one block case the comprehensive treatment plan had to be modified and the study site requested an additional surgical intervention leading to the exclusion from the study. In one block case the CBCT scanning was not adequately performed. Because of the unexpectedly long duration of the recruitment period, in August 2017, it was decided to interrupt the patient recruitment.

Twenty-four patients were included for the analysis. Of these, 12 were randomized to the block group and 12 to the particulate group. Patient gender, patient age and implant location are reported in Table A1. At 6 months, CBCT examination and re-entry surgery were performed in all 24 patients. All implants were clinically and radiographically osseointegrated.

Soft tissue condition

Two mucosal dehiscences were observed at the time of suture removal. One of these occurred in the particulate group and one in the block group. Moreover, at suture removal, there was 1 case of swollen mucosa in each group. At 4 weeks and at 6 months, the soft tissue condition was rated “normal” in all patients.

Bucco-oral hard tissue changes

The results of radiographically assessed hard tissue thickness changes are presented in Tables 1a and 1b.

Intraoperatively, the median horizontal thickness of DBBM measured 3 mm (mean±SD: 3.17±0.49 mm) in the block group and 4 mm (mean±SD: 4.00±0.74 mm) in the particulate group (Table 1a, Fig. 6).

After wound closure, the median horizontal thickness of the augmented hard tissue reached 3.35 mm (mean±SD: 3.38±0.59 mm) in the block group and 2.85 mm (mean±SD: 2.73 ± 0.69 mm) in the particulate group (Table 1a, Fig. 6).

At 6 months, the median horizontal thickness of the augmented hard tissue amounted to 2.90 mm (mean±SD: 2.71±1.19 mm) in the block group and 0.2 mm (mean±SD: 0.52±0.80 mm) in the particulate group (Table 1a, Fig. 6). The difference in HT at 6 months between the groups measured 2.7 mm and was statistically significant ($p<0.001$; 95% confidence interval: 1.1 mm; 3.0 mm).

Apico-coronal hard tissue changes

The median defect height clinically assessed after implant placement measured 3.5 mm in the block group and 4.25 mm in the particulate group ($p=0.749$) (Table 2).

At re-entry surgery, 11 out of 12 (91.7%) block sites and 3 out of 12 (25%) particulate sites clinically showed a complete vertical defect fill. The median vertical defect amounted to 0 mm in the block group and to 0.75 mm in the particulate group ($p = 0.001$) corresponding to median vertical defect resolutions of 100% (mean: 98.6%) and 87% (mean: 80.5%), respectively (Table 2).

In the 6-month CBCT, 12 out of 12 (100%) block sites and 8 out of 12 (66.7%) particulate sites showed a complete vertical defect fill. The differences between the observations in CBCT and at re-entry surgery were caused by DBBM particles within the mucosal flaps.

Discussion

The results of the present RCT demonstrated that the block of DBBM with NBCM was superior to particulate DBBM and NBCM with respect to the thickness of the augmented hard tissue after 6 months of healing. DBBM block maintained the augmented space better than particulate DBBM. This holds true both during wound closure and over the 6-month healing period.

With respect to the **dimensions of the augmented ridge**, the results of the present clinical trial confirm the findings of the recent **proof-of-the-principle** in-vitro and in-vivo **preclinical investigations** of individually shaped bone substitute blocks used for the augmentation of peri-implant bone defects (Benic, et al., 2017b; Benic, et al., 2016; Mir-Mari, et al., 2016). An **in-vitro** study assessed the horizontal dimensions of block and particulate DBBM in combination with CM prior to and after wound closure (Mir-Mari, et al., 2016). In this study, the following material combinations for the augmentation of peri-implant defects were assessed by means of CBCT: (i) particulate DBBM + NBCM, (ii) particulate DBBM + NBCM + fixation pins, and (iii) DBBM block + NBCM. The investigators found that wound closure induced a considerable displacement of particulate DBBM resulting in a partial collapse of the NBCM. The average reduction in the horizontal thickness at the implant shoulder amounted to 40% for particulate DBBM + NBCM without fixation pins. The sites augmented with DBBM block + NBCM without pins exhibited an average loss of thickness of 20% caused by the displacement of the block graft during wound closure. A similar average value of 20% in thickness reduction was achieved with particulate DBBM + NBCM + fixation pins. In the present clinical study, the sites augmented with particulate DBBM + NBCM + fixation pins lost approximately 30% in thickness during wound closure. This result is in accordance with the findings from the previous in-vitro CBCT study. On the other side, in the present study the sites augmented with DBBM block + NBCM + fixation pins were able to maintain the space during flap suturing. The difference between this finding and the results of the previous in-vitro CBCT study can be explained by the use of fixation pins in this clinical trial. A recent preclinical study assessed the **in-vivo** performance of a collagen-containing equine block, of a DBBM block and of particulate DBBM used for GBR with simultaneous implant placement (Benic, et al., 2017b). All the grafting materials were applied with CM without fixation pins for the augmentation of large peri-implant defects. After 4 months of healing, the equine block rendered the most favorable outcomes regarding hard tissue contours followed by the DBBM block and the particulate DBBM. The superior in-vivo

performance of block bone substitutes over particulate grafting material for the augmentation of deficient ridge contours was showed in another comparative preclinical trial (Schwarz, et al., 2008).

The use of individually shaped bone substitute blocks for the augmentation of peri-implant defects was assessed in a recent **clinical** study (Amorfini, Migliorati, Signori, Silvestrini-Biavati, Benedicenti, 2014). In this split-mouth RCT corticocancellous allograft blocks covered with CM were compared to a mixture of particulate DBBM and autogenous bone with CM. Osteosynthesis screws were used in both groups to stabilize the grafting materials. The variation of the hard tissue volume was measured by superimposing the preoperative CBCT with the CBCT taken after 1 year of healing. The block allograft and the particulate graft showed similar results regarding the augmented bone volume (Amorfini, et al., 2014). Due to the differences in the regions-of-interest and the outcome variables used for the assessment, the results from the investigation of the allograft block cannot be compared to the results of the present trial. In fact, in the previous RCT the entire volume of the augmented region was measured in mm^3, whereas in the present study the bucco-oral thickness of the augmented ridge was assessed specifically at the level of the implant shoulder. Another RCT assessed the horizontal hard tissue changes 6 months after augmentation of peri-implant defects with particulate DBBM (Naenni, et al., 2017). In 27 patients, 27 dental implants were placed in single-tooth gaps in the anterior and premolar area. The implants were placed at least 6 weeks after tooth extraction corresponding either to type 2, type 3 or type 4 procedures (Hammerle, Chen, Wilson, 2004). Buccal dehiscence and/or fenestration-type defects were augmented with particulate DBBM randomly covered either with a NBCM or a titanium-reinforced non-resorbable membrane. Tacks for the membrane fixation were used in both groups. The bucco-oral thickness of the augmented region was clinically measured during the surgical intervention and at re-entry surgery 6 month later. The mean horizontal thickness after augmentation measured 3.5 mm for the NBCM group. At re-entry, this value decreased to 1.3 mm on average. The considerable horizontal change at the level of the implant shoulder after 6 month reported by these investigators is in agreement with the observations from the present trial. However, in the present study the thickness reduction for the group particulate + NBCM + pins was more pronounced. The difference in the values of hard tissue thickness may be explained by different assessment modalities and time points of implant placement after tooth extraction. In particular, the previous study included the type 2 implant placement time point, which probably more often lead to contained 2-wall defects with less exposure to the pressure of the mucosal flap. In the present study all the implants were placed more than 4 months after

tooth extraction and the majority of the peri-implant defects were poorly contained 1-wall defects.

In the present study, at re-entry surgery, 11 out of 12 block sites and 3 out of 12 particulate sites clinically showed a complete vertical defect fill. This translated into 98.6% and 80.5% of mean **vertical defect resolution** in the block and particulate group, respectively. The dimensions of the remaining bone defects at re-entry ranged from 0.5 to 1 mm. In the previously mentioned RCT comparing CM and non-resorbable membranes in combination with particulate DBBM, 6 out of 13 sites with CM demonstrate incomplete vertical regeneration (Naenni, et al., 2017). The vertical defect resolution for particulate DBBM + CM + pins after 6 months amounted to 85%. Previous clinical studies with a similar design found dehiscence defect resolution for the combination of particulate DBBM and CM ranging from 91% to 96% (Jung, et al., 2003; Jung, Halg, Thoma, Hammerle, 2009; Zitzmann, Naef, Scharer, 1997). A recent systematic review on the efficacy of lateral bone augmentation at peri-implant defects included 28 clinical studies mostly using particulate xenograft and collagen membrane (Thoma et al., 2019). The meta-analysis rendered a mean vertical defect resolution of 81.3% ranging from 56.4% to 97.1%, which is in accordance with the results of the present study.

In the present study, **CBCT** was used for a standardized assessment of the change in the dimension of the augmented region. It is worth noting that the clinical measurement at re-entry surgery revealed more sites with remaining bone defects in comparison to the corresponding CBCT. At re-entry surgery, 1 out of 12 block sites and 3 out of 12 particulate sites showed remaining defect heights ranging from 0.5 to 2 mm. On the other hand, in CBCT only 4 particulate sites exhibited incomplete defect fill. The discrepancy between the clinical observation after flap elevation and the CBCT assessment can be explained by the DBBM particles within the mucosal flaps.

The results of the present investigations indicated that the use of block bone substitutes was more predictable than particulate grafting materials for a complete vertical defect fill and the contour augmentation at peri-implant bone defects. The use of customized bone substitute blocks for the augmentation of uncontained peri-implant bone defects has, therefore, the potential to eliminate the need for the use of non-resorbable materials, such as membranes, meshes or tenting screws. The results of this study demonstrate that the mechanical stability of a grafting material plays a significant role during wound closure as well as during the healing period. Due to the low sample size the results of the present 6-month investigation need to be interpreted with caution. Future long-term controlled clinical studies with baseline and follow-up measurements are needed to confirm or refute the findings of the present trial.

Conclusions

Within the limitations of the present preliminary analysis, it can be concluded that for GBR of poorly contained peri-implant defects:

- A block bone substitute in combination with a collagen membrane and fixation pins was superior to a particulate bone substitute with a collagen membrane and fixation pins with respect to the thickness of the augmented hard tissue after 6 months of healing.
- Despite the use of pins for membrane stabilization, considerable displacement of the particulate grafting material occurs both during flap suturing and during the subsequent healing period.
- The sites augmented with a block bone substitute exhibited less contour loss during wound closure and the 6-month healing period in comparison to the sites grafted with a particulate DBBM.
- The use of block bone substitute in combination with a collagen membrane was superior to a particulate bone substitute with a collagen membrane regarding the vertical bone defect resolution at the 6-month reentry.

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Conflict of interest

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Table legend

Table 1a. Results of the horizontal thickness of the augmented hard tissue

Table 1b. Results of the 45 degree-thickness of the augmented hard tissue

Table 2. Results of the defect height

Table A1. Patient demographics and distribution of implant locations.

Figure legend

Figure 1. (a, b) Bone dehiscence after implant placement. Guided bone regeneration with (c) particulate deproteinized bovine-derived bone mineral and (d) collagen membrane stabilized with polylactide pins. (e) CBCT bucco-oral images (left) immediately after wound closure and (right) after 6 months. (f) Incomplete vertical defect resolution at re-entry surgery, 6 months after implant placement.

Figure 2. (a, b) Bone dehiscence after implant placement. Guided bone regeneration with (c, d) an individually shaped block of deproteinized bovine-derived bone mineral and (e) collagen membrane stabilized with polylactide pins. (f) CBCT bucco-oral images (left) immediately after wound closure and (right) after 6 months. (g) Complete defect resolution and well maintained ridge contour at re-entry surgery, 6 months after implant placement.

Figure 3. CBCT bucco-oral images (left) immediately after wound closure and (right) 6 months after implant placement and GBR with an individually shaped block of deproteinized bovine-derived bone mineral and collagen membrane stabilized with polylactide pins (a) in the maxillary front and (b) in the maxillary premolar region.

Figure 4. CBCT bucco-oral images (left) immediately after wound closure and (right) 6 months after implant placement and GBR with particulate deproteinized bovine-derived bone mineral and collagen membrane stabilized with polylactide pins (a) in the maxillary front and (b) in the maxillary premolar region.

Figure 5. Horizontal thickness of the augmented hard tissue measured from the implant shoulder in a buccal direction (HT), and thickness of the augmented hard tissue measured in a bucco-coronal direction at 45 degrees to the implant long axis (45°T).

Figure 6. Boxplots representing the horizontal thickness of the augmented hard tissue at different time points. ° and * in the figure represent the outliers.

	Block (n=12)					Particulate (n=12)					p-value*
	Median	**Mean ± SD**	**IQR**	**Min**	**Max**	**Median**	**Mean ± SD**	**IQR**	**Min**	**Max**	
Intraoperative											
HT (mm)	3	3.17±0.49	0.5	2	4	4	4.00±0.74	0.5	3	5	0.007 †
Postoperative											
HT (mm)	3.35	3.38±0.59	0.7	2.4	4.3	2.85	2.73±0.69	0.5	1.2	4	0.017 †
6 months											
HT (mm)	2.90	2.71±1.19	0.8	0.2	4.2	0.2	0.52±0.80	0.5	0	2.4	<0.001 †
Change intraop-postop											
HT (mm)	0.25	0.22±0.45	0.6	-0.5	0.8	-1.1	-1.27±1.1	1.8	-3	0	<0.001 †
HT (%)	7.85	7.5±14.0	22.2	-13.3	26.7	-27.5	-28.9±23.2	32.7	-70.0	0	<0.001 †
Change postop-6m											
HT (mm)	-0.4	-0.68±0.82	0.6	-2.5	-0.1	-2.35	-2.21±0.98	1.3	-4	-0.6	<0.001 †
HT (%)	-11.9	-22.5±30.9	13.8	-91.7	-2.3	-92.7	-81.8±27.4	20.8	-100	-20	<0.001 †

*, Results of Mann-Whitney test; HT, horizontal thickness of the augmented hard tissue; intraop, intraoperative; postop, postoperative; 6m, 6 months; n, number; SD, standard deviation; IQR, interquartile range; Min, minimum; Max, maximum; †, statistically significant

Table 1a. Results of the horizontal thickness of the augmented hard tissue

	Block (n=12)					Particulate (n=12)					p-value*
	Median	**Mean ± SD**	**IQR**	**Min**	**Max**	**Median**	**Mean ± SD**	**IQR**	**Min**	**Max**	
Postoperative											
45°T (mm)	2.35	2.46±0.58	0.95	1.7	3.3	2.1	1.98±0.70	0.28	0.7	3.4	0.145
6 months											
45°T (mm)	1.75	1.61±0.93	1.5	0.1	2.8	0	0.33±0.65	0.2	0	1.8	<0.001 †
Change postop-6m											
45°T (mm)	-0.8	-0.85±0.61	1.1	-1.8	0	-1.9	-1.64±0.82	1.1	-3.2	-0.3	0.014 †
45°T (%)	-29.4	-38.1±32.0	35.3	-94.7	0	-100	-84.6±28.3	15.1	-100	-14.3	0.002 †

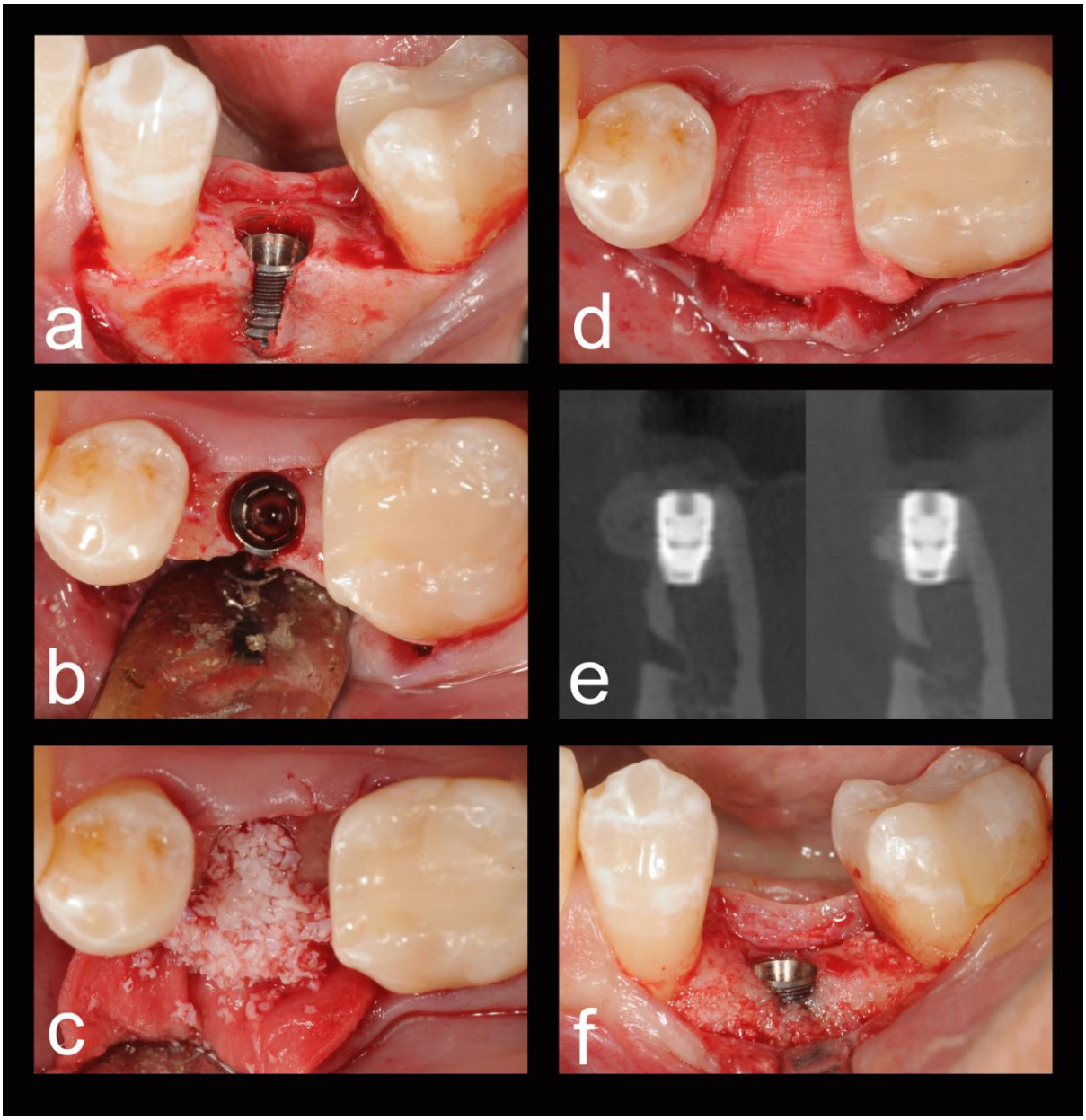
*, Results of Mann-Whitney test; 45°T, 45 degree-thickness of the augmented hard tissue; postop, postoperative; 6m, 6 months; ; n, number, SD, standard deviation, IQR, interquartile range; Min, minimum; Max, maximum; †, statistically significant

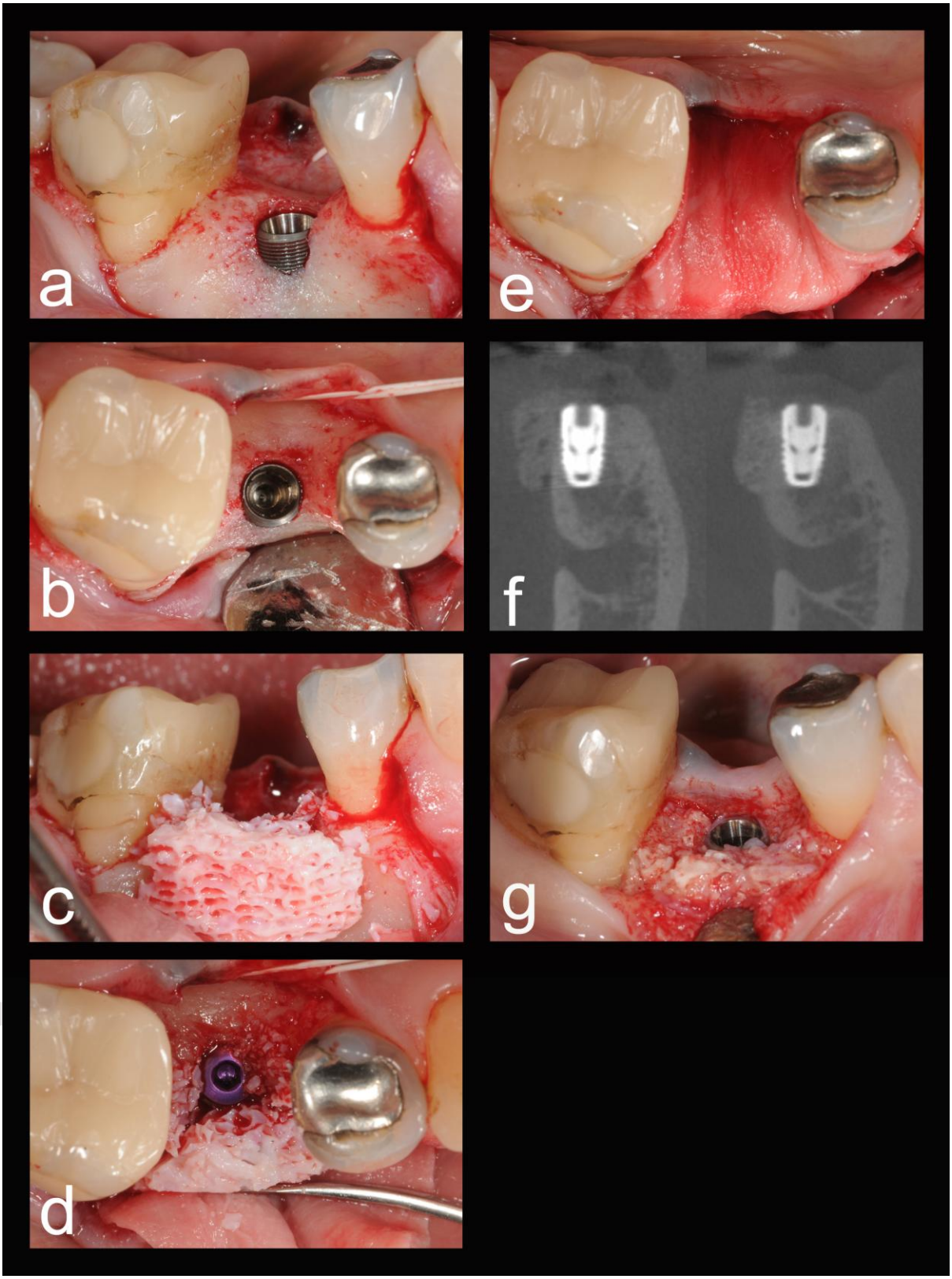
Table 1b. Results of the 45 degree-thickness of the augmented hard tissue

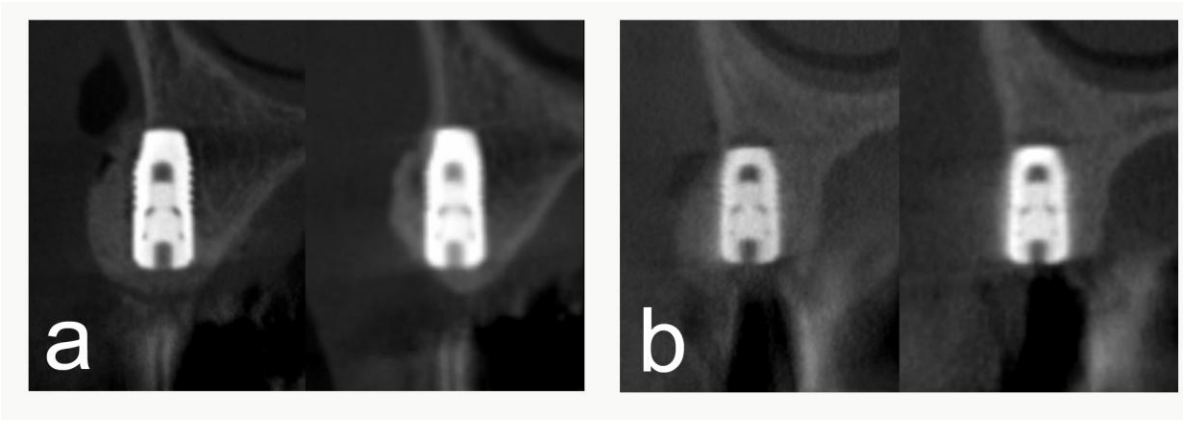
	Block (n=12)					Particulate (n=12)					p-value*
	Median	**Mean ± SD**	**IQR**	**Min**	**Max**	**Median**	**Mean ± SD**	**IQR**	**Min**	**Max**	
Intraoperative											
Defect height (mm)	3.5	4.54±2.50	4.1	2	9	4.25	4.58±2.12	2.5	2	8	0.749
6 months											
Defect height (mm)	0	0.04±0.14	0	0	0.5	0.75	0.75±0.62	0.6	0	2	0.001 †
Change intraop-6 months											
Defect height resolution (%)	100	98.6±4.8	0	83.3	100	86.6	80.5±18.5	31.0	50	100	0.002 †

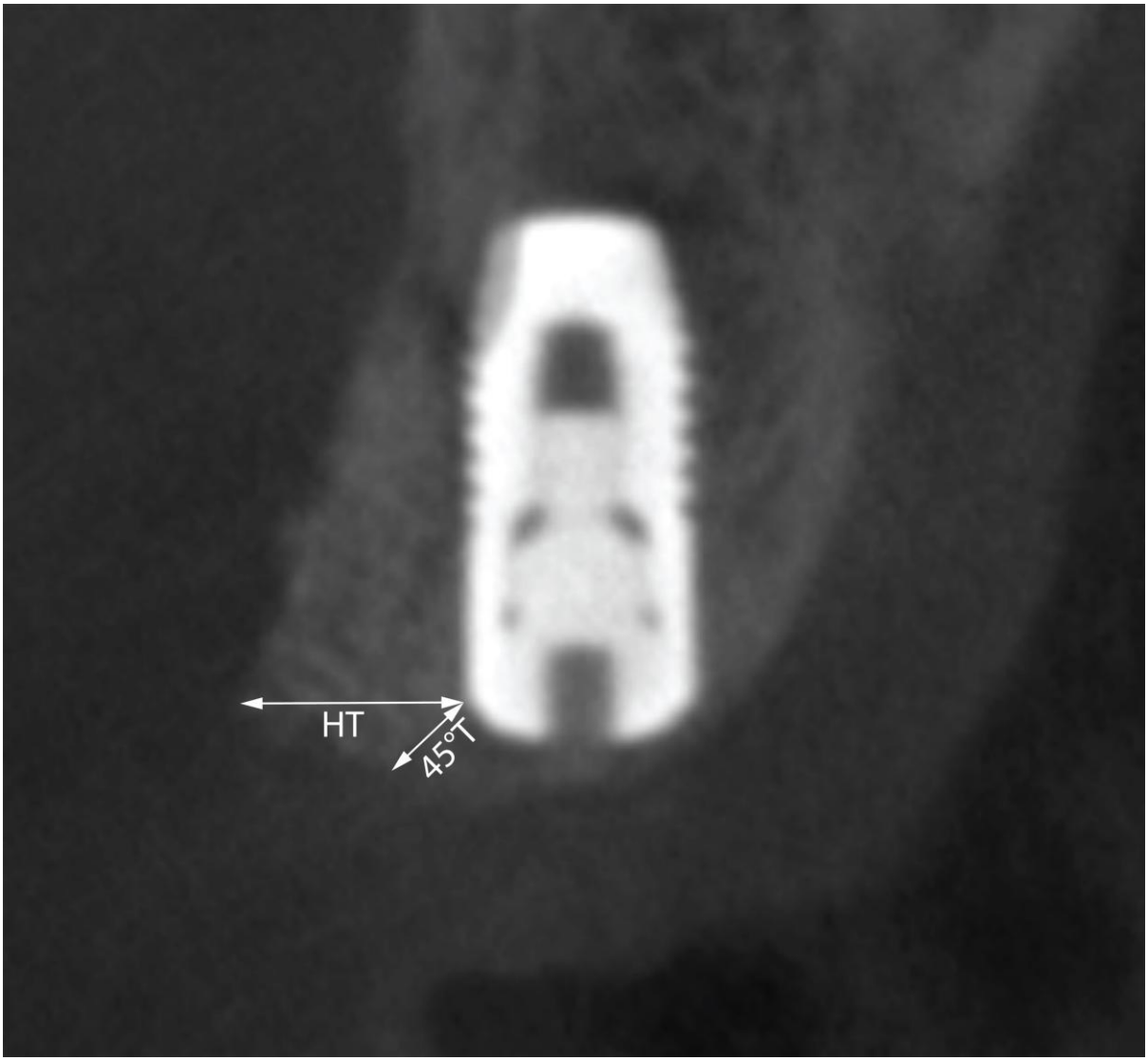
*, Results of Mann-Whitney test; n, number; SD, standard deviation; IQR, interquartile range; Min, minimum; Max, maximum; †, statistically significant

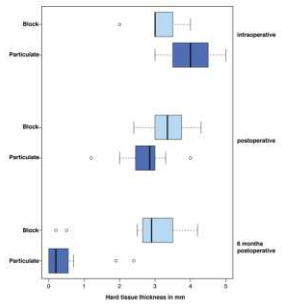
Table 2. Results of the defect height











	Block group	**Particulate group**
Gender (number)		
Female	7	7
Male	5	5
Age (years)		
Mean	62.0	58.1
Range	43.5 - 78.6	28.7 - 78.8
Median	62.8	62.2
Site (number)		
Incisive	4	0
Canine	0	3
Premolar	5	9
Molar	3	0
Jaw (number)		
Maxilla	7	6
Mandible	5	6

Table A1. Patient demographics and distribution of implant locations.